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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,967	01/21/2004	Tore Omtveit	NIDN-10365 CON	4085

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GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER

SCHLIENTZ, LEAH H

ART UNIT	PAPER NUMBER
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1618

MAIL DATE	DELIVERY MODE
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05/18/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/761,967

Applicant(s)

OMTVEIT ET AL.

Examiner

Leah Schlientz

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-39 is/are pending in the application.
- 4a) Of the above claim(s) 27 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-26, 28 and 30-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/775,959.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/21/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the following species: gold as the mixing surface and rotor stator as the mixing apparatus in the reply filed on 3/27/2007 is acknowledged. Claims 18 – 39 are pending, of which claims 27 and 29 are withdrawn from consideration as being drawn to non-elected species. Claims 18 – 26, 28, and 30 – 39 are readable upon the elected species.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18 – 26, 28, and 30 – 39 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 9 of U.S. Patent No. 6,444,193, in view of Earle (US 2,592,876).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a process for the preparation of a pharmaceutical composition comprising a gas precursor, vesicle membrane forming agent, lipids, etc. The process comprises the steps of subjecting a discontinuous water-immiscible phase and a continuous aqueous phase to shear forces exerted by first and second surfaces moving relative to each other at specific speeds, i.e. 20 m/s, 30 m/s, and 60 m/s. The moving surfaces require a rotor and a stator, and are separated by 100 to 500 μm . While the '139 patent does not specifically claim that the rotor stator mixer has a gold mixing surface, it would have been obvious to one of ordinary skill in the art to include such a coating on the mixing surfaces of the rotor stator of the '139 patent because Earle teaches that rotor stator mixers having a gold coating are known in the art to provide the benefit of substantial improvement in operation time of the apparatus when operated in fluid media (column 1). Such gold coatings are provided at a thickness of 0.0001 inches, for example (i.e. 2.54 μm).

Specification

The disclosure is objected to because of the following informalities: the date of the priority claim to Great Britain patent application 9818921.9 is incorrect. Currently,

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the date is August 1, 1988, rather than August 1, 1998. Appropriate correction is required.

The disclosure is objected to because of the following informalities: in many instances, the letter "E" has been used instead of the degree symbol ($^{\circ}$) in reference to temperatures and angles. For example, on page 3, line 2, "25EC" apparently should read "25 $^{\circ}$ C". See also, for example, page 5, line 27, "25EC"; page 5, line 28, "55E"; page 5, line 28, "45E"; page 5, line 29, "30E"; page 5, line 31, "26E"; page 5, line 33, "60E"; page 13, line 32, "25EC"; and page 14, line 7, "Contact angle (E)". Appropriate correction is required.

The disclosure is objected to because of the following informalities: in lines 20 and 21 of page 8, the sentence which reads "inventions are preferably fluids whereby The materials being mixed using the process of the emulsion, suspension or dispersion is produced on mixing." is objected to because it begins with a lower case letter, has "The" capitalized mid-sentence, and is generally incomprehensible. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30 – 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The originally filed disclosure does not specifically suggest the step of subjecting the discontinuous water-immiscible phase and the continuous aqueous phase to shear forces exerted by first and second surfaces moving relative to each other at a speed of at least 20 m/s, 30 m/s, or 60 m/s, wherein said first and second surfaces are gold plated. For example, the specification provides support only for a relative rotor:stator speed of at least 32 m/s, e.g. 46 m/s (see Example 2). This is a new matter rejection.

Claim 36 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The originally filed disclosure does not specify that moving gold plated surfaces are separated by from 100 to 500 μm . This is a new matter rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 18 – 26, 28 and 30 – 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Omtveit *et al.* (US 6,444,193).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Omtveit discloses a process for the preparation of gas-containing vesicles wherein a mixture of gas, liquid and vesicle membrane forming material is passed through a zone in which it is subject to shear forces exerted by surfaces moving relative to each other at a speed of up to 60 m/s (abstract and claim 3). The moving surfaces are separated by from 100 to 500 μm (claim 9). The rotors and stators of the mixing

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apparatus are gold plated (column 6, lines 24 – 25). Regarding claims 23 – 25, gold is inherently capable of interacting with materials in the claimed manner according to the instant specification (page 5, lines 25+).

Claims 18, 23 – 26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Acree (US 1,980,589).

Acree teaches processes of formation of suspensions and emulsions and apparatus and machinery designed to perform the processes (page 1, column 1, lines 1 – 6). By using albumins, gum arabic, oleic acid, sulphonated animal or vegetable oils, etc. and employing water, a wide variety of dispersions may be made, including medicines (page 7, column 1, lines 27 – 35). The apparatus includes a colloid mill (i.e. rotor stator) and may be plated with gold (page 4, column 1, lines 66 – 71). Regarding claims 23 – 25, gold is inherently capable of interacting with materials in the claimed manner according to the instant specification (page 5, lines 25+).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 18 – 20, 22 – 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert (US 5,552,133) in view of Earle (US 2,592,876).

Lambert discloses encapsulated gas microspheres useful as ultrasonic imaging agents made by mixing an aqueous solution of a heat-denaturable protein with a gas and passing the gas-solution through a mill whereby the mixture is emulsified near the denaturation temperature of the protein and subjected to mechanical shearing and cavitation which causes the formation of gas bubbles in the 0.2 to 10 micron range and the protein to locally denature and deposit at the gas-liquid interface to form encapsulated microspheres (abstract). After the gas and protein solution are combined, the mixture is emulsified and subjected to cavitation, which is accomplished via an apparatus such as a high speed mixer, preferably a colloid mill, which is a machine consisting of a high-speed rotor and stator (column 5, lines 12+). The rotor speed, gap size and gas:liquid ratio process parameters are adjusted empirically to provide a product having the desired characteristics (particle size, etc.) (column 6, lines 22 – 32).

Lambert does not teach a gold-plated rotor stator homogenizer.

Earle teaches a rotor and stator for fluid handling machines having surfaces coated with gold (column 1 and claim 1). Such gold coatings are provided at a thickness of 0.0001 inches, for example (i.e. 2.54 μm).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide a gold coating on the rotor stator mixer employed by Lambert in the preparation of microbubble suspensions. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Earle specifically teaches that rotor and stator devices having surfaces coated with gold are advantageous because such coatings substantially improve the operational time period for such bladed structures (rotor stators) which are intended for operation in fluid media as compared to uncoated structures (column 1).

Claims 18 – 20, 22 – 26, 28 and 30 – 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert (US 5,552,133) in view of Earle (US 2,592,876), in further view of Rourke (US 5,643,506) and Walz (US 5,959,001).

Lambert discloses encapsulated gas microspheres useful as ultrasonic imaging agents made by mixing an aqueous solution of a heat-denaturable protein with a gas and passing the gas-solution through a mill whereby the mixture is emulsified near the denaturation temperature of the protein and subjected to mechanical shearing and cavitation which causes the formation of gas bubbles in the 0.2 to 10 micron range and the protein to locally denature and deposit at the gas-liquid interface to form encapsulated microspheres (abstract). After the gas and protein solution are combined,

the mixture is emulsified and subjected to cavitation, which is accomplished via an apparatus such as a high speed mixer, preferably a colloid mill, which is a machine consisting of a high-speed rotor and stator" (column 5, lines 12+). The rotor speed, gap size and gas:liquid ratio process parameters are adjusted empirically to provide a product having the desired characteristics (particle size, etc.) (column 6, lines 22 – 32).

Lambert does not teach a gold-plated rotor stator homogenizer. In addition, while the high-speed rotor stator device disclosed by Lambert would be expected to have multiple zones and operate at speeds as claimed, the cited art fails to specifically teach the claimed zones and speeds.

However, gold-plated rotor stators, as well as rotor stator devices having multiple zones and which use speeds as claimed are well known in the art, as shown by Earle, Rourke, and Walz.

Earle teaches a rotor and stator for fluid handling machines having surfaces coated with gold, as set forth above. Such gold coatings are provided at a thickness of 0.0001 inches, for example (i.e. 2.54 μm).

Rourke discloses the use of high shear mixers having multiple zones that provide the advantage of providing microcapsules of uniform particle size (columns 1 – 3).

Walz teaches that rotor stator devices commonly used in the production of microparticles operate at speeds of up to 60 m/s (column 6, lines 26 – 32).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide a gold coating on the rotor stator mixer employed by Lambert in the preparation of microbubble suspensions. One would have been

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motivated to do so, and would have had a reasonable expectation of success in doing so, because Earle specifically teaches that rotor and stator devices having surfaces coated with gold are advantageous because such coatings substantially improve the operational time period for such bladed structures (rotor stators) which are intended for operation in fluid media as compared to uncoated structures (column 1). Furthermore, it would have been obvious to use multiple zones and various speeds in the methods of Lambert because it is well known in the art that such multiple zones and speeds provide advantages such as uniform particle size, as shown by Rourke and Walz. One would have been motivated to use such speeds because Lambert teaches such parameters as speed, etc. to be adjustable. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

Claims 18 – 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dugstad (WO 97/29783, whereby US 6,217,850 is relied upon) in view of Earle (US 2,592,876).

Dugstad discloses microbubble dispersions stabilized by phospholipids (abstract). The microbubbles, suitable for use as ultrasound contrast agents, are prepared by rotor stator mixing (see Example 2).

Dugstad does not teach a gold-plated rotor stator homogenizer.

Earle teaches a rotor and stator for fluid handling machines having surfaces coated with gold.

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It would have been obvious to one of ordinary skill in the art at the time of the instant invention to one of ordinary skill in the art at the time of the instant invention to provide a gold coating on the rotor stator mixer employed by Dugstad in the preparation of microbubble suspensions. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Earle specifically teaches that rotor and stator devices having surfaces coated with gold are advantageous because such coatings substantially improve the operational time period for such bladed structures (rotor stators) which are intended for operation in fluid media as compared to uncoated structures (column 1).

Conclusions

No claims are allowed at this time.

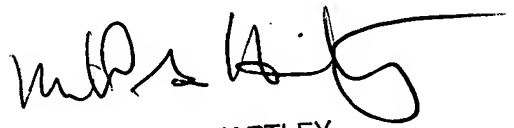
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS



MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER